

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A41347A	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2004/008786	International filing date (day/month/year) 16.06.2004	Priority date (day/month/year) 16.06.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant RIKEN		

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 22 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
 - ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - ☒ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s))
1 flexible disk, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

- This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:

- ☐ international search (Rule 12.3 and 23.1(b))
☐ publication of the international application (Rule 12.4)
☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ neither restricted the claims nor paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☐ complied with.
 - ☒ not complied with for the following reasons:

With regards to the fluorescent proteins that are represented by SEQ ID NO: 1, 3, 5, 7, 9, 11 and 13 set forth in the claims, although the fluorescent proteins derived from species of the genus *Acropora* which are represented by SEQ ID NO: 3, 5 and 7 have similar amino acid sequences (i.e. said proteins exhibit a homology of 88% or higher), there is no chemical structure that is common among the other amino acid sequences (i.e. said proteins exhibit a homology of 65% or lower); therefore, said proteins are only linked by the feature of being fluorescent proteins that are derived from species of the class *Anthozoa*.

[Refer to the Supplemental Box]

4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos. _____

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
1. Statement	
Novelty (N)	Claims <u>1-35</u> YES Claims _____ NO
Inventive step (IS)	Claims _____ YES Claims <u>1-35</u> NO
Industrial applicability (IA)	Claims <u>1-35</u> YES Claims _____ NO
2. Citations and explanations (Rule 70.7)	
Document 1:	WO 03/042401 A2 (Clontech Laboratories Inc.), 22 May 2003
Document 2:	WO 01/027150 A2 (Clontech Laboratories Inc.), 19 April 2001 & EP 1305412 A2 & JP 2003-527833 A
Document 3:	WO 02/068459 A2 (Clontech Laboratories Inc.), 06 September 2002 & EP 1385967 A2 & US 2002/0197676 A1 & US 2003/0022287 A1
Document 4:	WO 00/34318 A1 (Clontech Laboratories Inc.), 15 June 2000
Document 5:	JP 2002-531146 A (Clontech Laboratories Inc.), 24 September 2002 & WO 2000/34526 A1 & EP 1135532 A1
Document 6:	WO 00/34320 A1 (Clontech Laboratories Inc.), 15 June 2000
Document 7:	WO 02/090535 A1 (Rigel Pharmaceuticals Inc.), 14 November 2002 & EP 1399547 A1 & US 2003/0149254 A1 & US 2004/0002056 A1
Document 8:	WO 00/34319 A1 (Clontech Laboratories Inc.), 15 June 2000
Document 9:	WO 02/096924 A1 (Clontech Laboratories Inc.), 05 December 2002
Document 10:	WO 03/033693 A1 (The Institute of Physical

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and Chemical Research), 24 April 2003

Document 11: WO 00/34321 A1 (Clontech Laboratories Inc.),
15 June 2000

Claims 1, 7, 13 to 15, 26 to 30, 32, 34 and 35

The inventions set forth in claims 1, 7, 13 to 15, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 1 cited in the international search report.

Document 1 discloses the fluorescent protein zoanRFP, which comprises a 231 acid-long amino acid sequence that is derived from species of the genus *Zoanthus* (refer to fig. 10, SEQ ID NO: 5 and 6), and said amino acid sequence has a homology of 65% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Montipora*, which is represented by SEQ ID NO: 1 set forth in the present application.

However, the genus *Zoanthus* and the genus *Montipora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 1 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 1 and then searching the cDNA libraries from species of the genus *Montipora*.

Claims 1, 7, 13 to 15, 26 to 30, 32, 34 and 35

The inventions set forth in claims 1, 7, 13 to 15, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 2 cited in the international

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search report.

Document 2 discloses the fluorescent protein zFP506 (also known as NFP-3), which comprises a 231 acid-long amino acid sequence that is derived from species of the genus *Zoanthus* (refer to fig. 3, SEQ ID NO: 5 and 6), and said amino acid sequence has a homology of 63% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Montipora*, which is represented by SEQ ID NO: 1 set forth in the present application.

However, the genus *Zoanthus* and the genus *Montipora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 1 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 1 and then searching the cDNA libraries from species of the genus *Montipora*.

Claims 6, 12, 13, 24 to 30, 32, 34 and 35

The inventions set forth in claims 6, 12, 13, 24 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 2 cited in the international search report.

Document 2 discloses the fluorescent protein cFP484 (also known as NFP-2), which comprises a 266 acid-long amino acid sequence that is derived from species of the genus *Clavularia* (refer to fig. 2, SEQ ID NO: 3 and 4), and said amino acid sequence has a homology of 81% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Sarcophyton*,

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which is represented by SEQ ID NO: 13 set forth in the present application.

However, the genus *Clavularia* and the genus *Sarcophyton* belong to the same subclass (i.e. the subclass *Octocorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 13 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 2 and then searching the cDNA libraries from species of the genus *Sarcophyton*.

Claims 1, 7, 13 to 15, 26 to 30, 32, 34 and 35

The inventions set forth in claims 1, 7, 13 to 15, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 3 cited in the international search report.

Document 3 discloses the fluorescent protein zFP506 (also known as NFP-3), which comprises a 231 acid-long amino acid sequence that is derived from species of the genus *Zoanthus* (refer to fig. 2, SEQ ID NO: 3 and 4), and said amino acid sequence has a homology of 63% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Montipora*, which is represented by SEQ ID NO: 1 set forth in the present application.

However, the genus *Zoanthus* and the genus *Montipora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 1 set forth in

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the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 3 and then searching the cDNA libraries from species of the genus *Montipora*.

Claims 2, 3, 8, 9, 13, 16 to 19, 26 to 30, 32, 34 and 35

The inventions set forth in claims 2, 3, 8, 9, 13, 16 to 19, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 3 cited in the international search report.

Document 3 discloses the fluorescent protein amFP486 (also known as NFP-1), which comprises a 229 acid-long amino acid sequence that is derived from the species *Anemonia majano* (refer to fig. 1, SEQ ID NO: 1 and 2), and said amino acid sequence has a homology of 64%, 61% and 63%, respectively, in relation to the amino acid sequences of the fluorescent proteins derived from species of the genus *Acropora*, which are represented by SEQ ID NO: 3, 5 and 7 set forth in the present application.

However, the species *Anemonia majano* and species of the genus *Acropora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the genes which code the fluorescent proteins that are represented by SEQ ID NO: 3, 5 and 7 set forth in the present application by creating degenerate primers or probes based on the sequence information that is disclosed in document 3 and then searching the cDNA libraries from species of the genus *Acropora*.

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Claims 4, 10, 13, 20, 21, 26 to 30, 32, 34 and 35

The inventions set forth in claims 4, 10, 13, 20, 21, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 3 cited in the international search report.

Document 3 discloses the fluorescent protein zFP506 (also known as NFP-3), which comprises a 231 acid-long amino acid sequence that is derived from species of the genus *Zoanthus* (refer to fig. 2, SEQ ID NO: 3 and 4), and said amino acid sequence has a homology of 81% in relation to the amino acid sequence of the fluorescent protein from species of the genus *Montipora*, which is represented by SEQ ID NO: 9 set forth in the present application.

However, the genus *Zoanthus* and the genus *Montipora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 9 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 3 and then searching the cDNA libraries from species of the genus *Montipora*.

Claims 1, 4, 7, 10, 13 to 15, 20, 21, 26 to 30, 32, 34 and 35

The inventions set forth in claims 1, 4, 7, 10, 13 to 15, 20, 21, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 4 cited in the international search report.

Document 4 discloses the fluorescent protein

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zFP506, which comprises a 230 acid-long amino acid sequence that is derived from species of the genus *Zoanthus* (refer to SEQ ID NO: 56), and said amino acid sequence has a homology of 64% and 81% in relation to the amino acid sequences of the fluorescent proteins derived from species of the genus *Montipora*, which are represented by SEQ ID NO: 1 and 9 set forth in the present application.

However, the genus *Zoanthus* and the genus *Montipora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the genes which code the fluorescent proteins that are represented by SEQ ID NO: 1 and 9 set forth in the present application by creating degenerate primers or probes based on the sequence information that is disclosed in document 4 and then searching the cDNA libraries from species of the genus *Montipora*.

Claims 2, 3, 8, 9, 13, 16 to 19, 26 to 30, 32, 34 and 35

The inventions set forth in claims 2, 3, 8, 9, 13, 16 to 19, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 5 cited in the international search report.

Document 5 discloses the fluorescent protein amFP486, which comprises a 229 acid-long amino acid sequence that is derived from the species *Anemonia majano* (refer to SEQ ID NO: 55), and said amino acid sequence has a homology of 64%, 63% and 63%, respectively, in relation to the amino acid sequences of the fluorescent proteins derived from species of the genus *Acropora*, which are represented by SEQ ID NO: 3, 5 and 7 set forth in the present application.

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However, the species *Anemonia majano* and species of the genus *Acropora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the genes which code the fluorescent proteins that are represented by SEQ ID NO: 3, 5 and 7 set forth in the present application by creating degenerate primers or probes based on the sequence information that is disclosed in document 5 and then searching the cDNA libraries from species of the genus *Acropora*.

Claims 4, 10, 13, 20, 21, 26 to 30, 32, 34 and 35

The inventions set forth in claims 4, 10, 13, 20, 21, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 5 cited in the international search report.

Document 5 discloses the fluorescent protein zFP506, which comprises a 230 acid-long amino acid sequence that is derived from species of the genus *Zoanthus* (refer to SEQ ID NO: 57), and said amino acid sequence has a homology of 81% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Montipora*, which is represented by SEQ ID NO: 9 set forth in the present application.

However, the genus *Zoanthus* and the genus *Montipora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 9 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 5 and then searching the cDNA

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libraries from species of the genus *Montipora*.

Claims 5, 11, 13, 22, 23 and 26 to 35

The inventions set forth in claims 5, 11, 13, 22, 23 and 26 to 35 do not involve an inventive step in the light of document 5 cited in the international search report.

Document 5 discloses the fluorescent protein asFP600, which comprises a 232 acid-long amino acid sequence that is derived from the species *Anemonia sulcata* (refer to SEQ ID NO: 61), and said amino acid sequence has a homology of 69% in relation to the amino acid sequence of the fluorescent protein derived from the species *Anemonia erythraea*, which is represented by SEQ ID NO: 11 set forth in the present application.

However, the species *Anemonia sulcata* and the species *Anemonia erythraea* belong to the same sub-order (i.e. the sub-order Actiniidae); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 11 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 5 and then searching the cDNA library from the species *Anemonia erythraea*.

Claims 2, 3, 8, 9, 13, 16 to 19, 26 to 30, 32, 34 and 35

The inventions set forth in claims 2, 3, 8, 9, 13, 16 to 19, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 6 cited in the international search report.

Document 6 discloses the fluorescent protein

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amFP486, which comprises a 229 acid-long amino acid sequence that is derived from the species *Anemonia majano* (refer to SEQ ID NO: 55 and 56), and said amino acid sequence has a homology of 64%, 63% and 63%, respectively, in relation to the amino acid sequences of the fluorescent proteins are derived from species of the genus *Acropora*, which are represented by SEQ ID NO: 3, 5 and 7 set forth in the present application.

However, the species *Anemonia majano* and species of the genus *Acropora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the genes which code the fluorescent proteins that are represented by SEQ ID NO: 3, 5 and 7 set forth in the present application by creating degenerate primers or probes based on the sequence information that is disclosed in document 6 and then searching the cDNA libraries from species of the genus *Acropora*.

Claims 4, 10, 13, 20, 21, 26 to 30, 32, 34 and 35

The inventions set forth in claims 4, 10, 13, 20, 21, 26 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 7 cited in the international search report.

Document 7 discloses the fluorescent protein zFP5, which comprises a 231 acid-long amino acid sequence that is derived from species of the genus *Zoanthus* (refer to fig. 1), and said amino acid sequence has a homology of 81% in relation to the amino acid sequence of the fluorescent protein is derived from species of the genus *Montipora*, which is represented by SEQ ID NO: 9 set forth in the present application.

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However, the genus *Zoanthus* and the genus *Montipora* belong to the same subclass (i.e. the subclass *Hexacorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 9 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 7 and then searching the cDNA libraries from species of the genus *Montipora*.

Claims 6, 12, 13, 24 to 30, 32, 34 and 35

The inventions set forth in claims 6, 12, 13, 24 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 7 cited in the international search report.

Document 7 discloses the fluorescent protein FP48, which comprises a 231 acid-long amino acid sequence that is derived from species of the genus *Clavularia* (refer to fig. 1), and said amino acid sequence has a homology of 81% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Sarcophyton*, which is represented by SEQ ID NO: 13 set forth in the present application.

However, the genus *Clavularia* and the genus *Sarcophyton* belong to the same subclass (i.e. the subclass *Octocorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 13 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 7 and then searching the cDNA libraries from species of the genus

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Sarcophyton.

Claims 5, 11, 13, 22, 23 and 26 to 35

The inventions set forth in claims 5, 11, 13, 22, 23 and 26 to 35 do not involve an inventive step in the light of document 8 cited in the international search report.

Document 8 discloses the fluorescent protein asFP600, which comprises a 232 acid-long amino acid sequence that is derived from the species *Anemonia sulcata* (refer to SEQ ID NO: 56), and said amino acid sequence has a homology of 69% in relation to the amino acid sequence of the fluorescent protein derived from the species *Anemonia erythraea*, which is represented by SEQ ID NO: 11 set forth in the present application.

However, the species *Anemonia sulcata* and the species *Anemonia erythraea* belong to the same sub-order (i.e. the sub-order *Actiniidae*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 11 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 8 and then searching the cDNA library from the species *Anemonia erythraea*.

Claims 5, 11, 13, 22, 23 and 26 to 35

The inventions set forth in claims 5, 11, 13, 22, 23 and 26 to 35 do not involve an inventive step in the light of document 9 cited in the international search report.

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Document 9 discloses the fluorescent protein asFP595, which comprises a 232 acid-long amino acid sequence that is derived from the species *Anemonia sulcata* (refer to fig. 1 and SEQ ID NO: 1 and 2), and said amino acid sequence has a homology of 69% in relation to the amino acid sequence of the fluorescent protein derived from the species *Anemonia erythraea*, which is represented by SEQ ID NO: 11 set forth in the present application.

However, the species *Anemonia sulcata* and the species *Anemonia erythraea* belong to the same sub-order (i.e. the sub-order *Actiniidae*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 11 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 9 and then searching the cDNA library from the species *Anemonia erythraea*.

Claims 6, 12, 13, 24 to 30, 32, 34 and 35

The inventions set forth in claims 6, 12, 13, 24 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 10 cited in the international search report.

Document 10 discloses a fluorescent protein, which comprises a 225 acid-long amino acid sequence that is derived from the species *Galaxea fascicularis* (refer to sequence 1), and said amino acid sequence has a homology of 81% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Sarcophyton*, which is represented by SEQ ID NO: 13 set

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forth in the present application.

However, the species *Galaxea fascicularis* and species of the genus *Sarcophyton* belong to the same subclass (i.e. the subclass *Octocorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 13 set forth in the present application by creating a degenerate primer or probe based on the sequence information that is disclosed in document 10 and then searching the cDNA libraries from species of the genus *Sarcophyton*.

Claims 6, 12, 13, 24 to 30, 32, 34 and 35

The inventions set forth in claims 6, 12, 13, 24 to 30, 32, 34 and 35 do not involve an inventive step in the light of document 11 cited in the international search report.

Document 11 discloses a fluorescent protein, which comprises a 266 acid-long amino acid sequence that is derived from species of the genus *Clavularia* (refer to sequence 56), and said amino acid sequence has a homology of 81% in relation to the amino acid sequence of the fluorescent protein derived from species of the genus *Sarcophyton*, which is represented by SEQ ID NO: 13 set forth in the present application, which is derived from species of the genus *Sarcophyton*.

However, the genus *Clavularia* and the genus *Sarcophyton* belong to the same subclass (i.e. the subclass *Octocorallia*); therefore, it can be considered to have been easy to clone the gene which codes the fluorescent protein that is represented by SEQ ID NO: 13 set forth in the present application by creating a

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degenerate primer or probe based on the sequence
information that is disclosed in document 11 and then
searching the cDNA libraries from species of the genus
Sarcophyton.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 34 includes the disclosure "1 to 4, 6, 7 to 10 or 12." However, it is not clear that the claim in question is citing other claims.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
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 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box. IV

However, fluorescent proteins that are derived from species of the class *Anthozoa* (subclass *Octocorallia* or subclass *Hexacorallia*) are well known, as disclosed in documents 1 to 11 indicated below; therefore, the feature of being a fluorescent protein that is derived from species of the class *Anthozoa* cannot be said to be a special technical feature in the meaning of PCT Rule 13.2.

Therefore, the inventions pertaining to the fluorescent proteins that are represented by SEQ ID NO: 1, 3, 5, 7, 9, 11 and 13 among the inventions that are set forth in the claims cannot be said to be a group of inventions that are so linked as to form a single general inventive concept, and although the fluorescent proteins that are represented by SEQ ID NO: 3, 5 and 7 conform to the requirement of unity of invention, the group of inventions in question can be considered to comprise five inventions that correspond to the five different types of fluorescent proteins.

Document 1: WO 03/042401 A2 (Clontech Laboratories Inc.), 22 May 2003

Document 2: WO 01/027150 A2 (Clontech Laboratories Inc.), 19 April 2001 & EP 1305412 A2 & JP 2003-527833 A

Document 3: WO 02/068459 A2 (Clontech Laboratories Inc.), 06 September 2002 & EP 1385967 A2 & US 2002/0197676 A1 & US 2003/0022287 A1

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/008786

Supplemental Box

Document 4: WO 00/34318 A1 (Clontech Laboratories Inc.),
15 June 2000

Document 5: JP 2002-531146 A (Clontech Laboratories
Inc.), 24 September 2002 & WO 2000/34526 A1
& EP 1135532 A1

Document 6: WO 00/34320 A1 (Clontech Laboratories Inc.),
15 June 2000

Document 7: WO 02/090535 A1 (Rigel Pharmaceuticals
Inc.), 14 November 2002 & EP 1399547 A1 &
US 2003/0149254 A1 & US 2004/0002056 A1

Document 8: WO 00/34319 A1 (Clontech Laboratories Inc.),
15 June 2000

Document 9: WO 02/096924 A1 (Clontech Laboratories
Inc.), 05 December 2002

Document 10: WO 03/033693 A1 (The Institute of Physical
and Chemical Research), 24 April 2003

Document 11: WO 00/34321 A1 (Clontech Laboratories Inc.),
15 June 2000

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